REMARKS

Claims 1-22 currently are pending. Claims 5-8, 11-12, 15-16 and 20-22 have been withdrawn from consideration

The examiner stated that the oath/declaration is defective because non-initialed and/or non-dated alterations have been made to it. To overcome the objection, applicants will submit a supplemental declaration in accordance with 37 CFR 1.67(a) (2).

Regarding the trademarks Gene Clean and PCR-Script, they represent a "kit for purifying DNA fragments from agarose gels" and a "vector system for cloning blunt end PCR fragments," respectively. Product information is available at http://www.qbiogene.com/technical/protocols/dna-kits or http://www.stratagene.com/products.

Claims 1-4 and 9-10 were rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. The examiner believes applicants do not describe DNA sequences encoding DOXS or HPPD that hybridize to SEQ ID NO: 1 or SEQ ID NO: 5 or any other DOXS or HPPD encoding DNA sequence other than those encoding DOCS from *Arabidopsis* of SEQ ID NO: 1, from *E. coli* of SEQ ID NO: 3. Also, the examiner believes applicants fail to describe a representative number of DOXS or HPPD encoding polynucleotides. The examiner also rejected the claims under the enablement requirement. The examiner believes that because of the lack of guidance in the present specification, undue trial and error experimentation would be required for one of ordinary skill in the art to make and use the present invention.

The use claims have been deleted or replaced by claims falling into a proper statutory

category.

As basis for the rejection under 35 USC § 112, first paragraph, the examiner cites *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir.1997). The subject patent '525 in *Lilly* relates to recombinant plasmids and microorganisms that produce vertebrate insulin. Accordingly, claim 1 of said patent was directed to a recombinant plasmid containing within its nucleotide sequence a cDNA which encodes for vertebrate insulin and claim 2 was directed to a recombinant organism containing within its nucleotide sequence a cDNA which codes for vertebrate insulin.

The Federal Circuit held in *Lilly*:

a) that a patent specification which includes by example a process for obtaining human insulin-encoding cDNA, and which describes the protein (amino acid sequence) that the cDNA encodes, but which does not describe the structure of the claimed cDNA in terms of its nucleotide sequence, does not comply with the written description requirement of 35 USC § 112, first paragraph.

b) that the cDNA nucleotide sequence for rat insulin, as described by the patentee, did not provide a written description adequate to claim the genus of vertebrate or mammalian insulin cDNA.

c) that the description in the respective patent of the amino acid sequences of the A and B chains constituting human insulin does not provide a written description of cDNA encoding for human insulin. This is because the structure of the protein itself is insufficient to positively determine the nucleotide structure of the corresponding natural DNA due to degeneracy of the genetic code.

However, the characteristics described in a)-c) above do not apply to the present application because the claimed subject matter relates to: a **method for producing plant** with increased tocopherol, vitamin K, chlorophyll and/or carotenoid contents which comprises e.g. expressing a DNA sequence coding for a 1-deoxy-D-xylulose-5-phosphate synthase in plants.

The invention of the present application is the finding that the over expression of a DNA encoding for a DOXS alone or in combination with a DNA encoding for HPPD in transgenic plants leads to an increase in the tocopherol, vitamin K, chlorophyll and/or carotenoid content.

Therefore, the present application teaches a method for overruling a limited step (metabolic bottleneck) in the production of the described metabolites. It is important to realize that each DNA- independently from its DNA sequence- can be used for this method as long as the DNA encodes for a protein with a DOXS and HPPD activity, respectively.

In light of the above, applicants traverse the rejections of claims 1-4 and 9-10 under 35 USC § 112, first paragraph.

Assay systems to measure DOXS and HPPD activity were state of the art and known to the skilled artisan at the priority date of the application at hand. In the specification the reaction catalyzed by the DOXS is described and relevant publications have been cited describing the cloning of genes encoding for DOXS and HPPD from various organisms and the biochemical characterization of the corresponding proteins (specification page 4, lines 32-40: Schwender et al., Arigoni et al., Lange et al., Lichtenthaler et al.). The cited publication Lange et al. contains a cross-reference to a document describing an assay for identifying DOXS protein encoding DNA sequences (Lois et al. *Proc. Natl. Acad. Sci. USA* Vol. 95, pp. 2105-2110, March 1998).

Moreover, a simple assay to identify DNA sequences or cDNA clones with HPPD activity is described by Denoya et al. This document is cited in the specification of the application at hand on page 7, lines 34-35. Hence, in light of the specification of the application at hand and the knowledge present in the prior art at the priority date of the present invention, the skilled artisan was undoubtedly able to identify DNA sequences encoding for DOXS or HPPD proteins, respectively.

The examiner stated that the specification fails to provide an adequate written description to support the genus of DNA sequence encoding proteins having DOXS or HPPD activity encompassed by the hybridization language as set forth in the claims.

As specified by the claims, the subject matter of the claims is directed to a **method for producing plants** with increased e.g. tocopherol content by using genes encoding proteins with DOXS or HPPD activity. Consequently, DNA sequences that do not encode for an active DOXS or HPPD protein, although they might hybridize with the disclosed DNA sequences, cannot be employed for the inventive method and are not covered by the subject matter of the set of claims. On the other hand, as already mentioned, each DNA sequences encoding for an active DOXS protein can be used for the inventive method.

The claimed subject matter of the application at hand is a method that employs genes encoding for DOXS or HPPD proteins for producing transgenic plants with altered metabolite levels. Beside the genes disclosed in the specification and the examples, gene from different sources can be used accordingly, as long as they encode for an active DOXS or HPPS protein. However, none of the claims is directed towards unknown DNA sequences that encode either

DOXS or HPPD proteins from any source. Therefore, it is absolutely not necessary to require that the present invention should disclose a teaching which goes far beyond the scope of the claimed subject matter, namely the isolation of unknown DOXS or HPPD sequences. Nevertheless, at the priority date of the present invention, a broad range of molecular and biochemical methods and techniques were available and well-known to the persons skilled in the art to isolate genes encoding for a certain activity on the basis of homologous DNA sequences and/or activity assays.

In sum, upon consideration of the fact that a) the present application claims a **method** which uses DOXS or DOXS and HPPD proteins for the manipulation of the plant metabolism; and that b) methods and techniques for the isolation of additional DNA sequences encoding for orthologs or paralogs of the DOXS or HPPD proteins and c) assay system to identify DNA sequences with DOXS or HPPD activity were already available and well-known to a skilled person at the priority date of the present application, applicants do not why one of ordinary skill in the art would have to undergo undue experimentation to make and use the present invention.

Claims 1-2, 9-10, 13-14 and 17-18 are rejected under 35 USC § 102(b)/103(a) as being anticipated by Mandel et al. in light of Estevez et al. The examiner believes Mandel teaches CLA1, a gene isolated using a fragment of a mutant CLA1 gene of an albino tDNA insertion mutant of *Arabidopsis (cla 1)* that was deficient in chlorophyll and carotenoids. Estevez teaches that CLA1 encodes a 1-deoxyxylulose-5-phosphate synthase of SEQ ID NO: 1. The examiner believes Mande further teaches complementation of the *cla Arabidopsis* mutant via *Agrobacterium*-mediated transformation that resulted in dramatic increases in the levels of

chlorophyll and carotenoids.

According to 35 USC § 102(b) a person shall be entitled to a patent unless the invention was patented or described in a printed publication..., **more than one year** prior to the date of application for patent in the United States. The 102(b) date of present application is September 17, 2001. Estevez et al. was published in September 2000. Therefore, the article by Estevez was **not** published more than one year prior to the date of application of the invention at hand for a US patent and cannot be the basis for a rejection under 35 USC § 102(b).

Furthermore, in the publication by Estevez et al. the invention of the application at hand was not described/disclosed nor rendered obvious. Estevez et al. teaches solely that the *cla1* gene encodes a DOXS protein of SEQ ID NO: 1. Moreover, the rejected claims cannot be considered as being made obvious by Mandel et al. in light of Estevez et al. for the following reasons. First, Estevez is not prior art for the purpose of 103(a) (see above). Also, Mandel et al. teaches that the phenotype of the *cla1* mutant can be recovered to the wild type level by complementation with a functional allele of the *cla1* gene. The complementation technique is and can be used in the art only to verify the nature of a certain mutation. This technique does not reveal any information about possible metabolic "bottlenecks" with respect to the increase of a certain metabolite above wild type level. It is well-known to the skilled artisan, that the reduction of a certain metabolite as a consequence of a reduced gene expression rate of a given gene (due to a mutation, antisense manipulation or co-suppression) does not allow the reverse conclusion, namely that overproduction of the same gene will lead to an increase in the metabolite of interest above wild-type level. Therefore, a skilled artisan would never regard the

results disclosed by Mandel et al., even in light of the teaching disclosed by Estevez et al, as a process for producing plants with increased metabolite levels compared to untreated wild type plants, which are the starting material for the present inventive method.

It is important to understand that the complementation of the *cla 1* mutant recovered only the wild-type phenotype, which has to be regarded as the level of an unmodified plant. In the application at hand, it is clearly indicated at page 26, lines 3-9, that the increase in tocopherol, vitamin K, chlorophyll and/or carotenoid content through functional over expression of the inventive genes means the articially acquired capability of increased biosynthesis of said metabolites compared to plants which have not been genetically modified. In other words, the present method allows the increase of the above-mentioned metabolites to levels **above** the wild type level.

To establish *prima facie* obviousness, the examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each claim element (*see, e.g., In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). The examiner has not met these requirements.

Claims 1-4, 9-10, 13-14 and 17-19 are rejected under 35 USC § 103(a) as being unpatentable over Mandel et al. in view of Dellapenna and further in view of Estevez.

Applicants believe one of ordinary skill in the art would not regard the results disclosed by Mandel et al., even in light of the teaching of Estevez et al., as a process for producing plants

with increased metabolite levels in comparison to untreated wild type plants. Dellapenna et al. is completely silent with respect to the use of a gene encoding for a DOXS protein for the production of transgenic plants with increased vitamin E content.

The examiner therefore has not established a *prima facie* case of obviousness. To establish *prima facie* obviousness, the examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each claim element (*see, e.g., In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)).

Applicants request a two months extension of time.

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Respectfully submitted,
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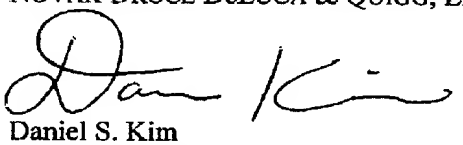

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